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5th Edition

COVID-19 Report

Finding the evidence for you

A weekly report to answer clinically relevant questions by summarizing the most recent evidence.

This information is intended for health care professionals.

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Clinical Description & Epidemiology

What specific comorbidities are associated with increase risk of severe disease in COVID-19?

- Cardiovascular disease, underlying respiratory disease, and hypertension were noted early in the course of the COVID-19 pandemic to be risk factors for severe disease (see [March 21, 2020 Newsletter](#)).
- Recent descriptive studies using national data from China and the United States have identified older age, malignancy, multiple comorbidities, and diabetes as consistent risk factors for severe disease.^{1,2,3} Worse outcomes are also seen in immunocompromised patients and those with renal disease.^{1,2} A recent New York area study reviewed over 4,000 cases of COVID-19 found obesity to be a risk factor for severe disease.³
- It should be noted that descriptive studies can be limited by the comorbidities selected for inclusion in the analysis.

Is the SARS-CoV-2 infection rate likely to vary with the changing of seasons or weather? What is the viability of SARS-CoV-2 at different temperatures?

- Coronaviruses, in general, tend to have a seasonal pattern of infection. For SARS-CoV-2, a study using modelling and statistical analysis has suggested that rising temperature may lower transmission in the Northern Hemisphere in the coming months.¹

- In one laboratory study, a reduction in SARS-CoV virus strain infectivity was observed at high temperatures (38°C with >95% relative humidity).² In another study, inactivation of SARS-CoV-2 was shown at 56°C and 70°C after 30 mins and 5 mins incubation, respectively.³
- Respiratory viruses remain stable and transmissible at low relative humidity (RH) and low temperature. Interestingly, more rapid viral inactivation is observed at a moderate RH of ~50% (typical in summer afternoons) compared to a low RH (20%) or high RH (80%). This might explain why areas in China with high humidity still saw high transmission of SARS-CoV-2.⁴
- It is difficult to predict the impact of seasonal variations in temperature and humidity on the future course of SARS-CoV-2. Factors such as herd immunity, host behavior, and infection control measures will all play a role in altering the trajectory of the pandemic.⁵

What is the estimated case fatality rate of COVID-19? Is this different for healthcare workers vs. the general population?

- Canada's COVID-19 case fatality rate (CFR) is 3.1% as of April 14th.¹ A preprint meta-analysis of 29 international studies reported an adjusted CFR of 7.4%.²
- The CDC recently reported an American healthcare worker CFR of 0.3% compared to 3.6% in the general population.³ A study of 72,315 COVID-19 patients in China also described a healthcare worker CFR lower than the general population (0.3% vs. 2.3%).⁴
- CFR is difficult to calculate in rapidly evolving pandemics such as COVID-19, due to biases introduced through diagnostics, surveillance, and analytic variability.² Thus far, initial reports indicate that healthcare worker CFR may be lower than the general population, but this may be related to differences in testing as well as underlying characteristics of the affected population.

Are there thrombotic complications associated with COVID-19? What are they and how commonly are they seen?

- Several reports indicate that abnormal coagulation parameters including elevated D-dimer and fibrin degradation products, prolonged prothrombin time, and thrombocytopenia often occur in COVID-19. ^{1,2,3,4,5} They are also associated with increased disease severity, development of ARDS, and mortality.
- Severe COVID-19 appears to be associated with high rates of thrombotic events. In a descriptive study of 184 ICU patients with COVID-19 from three Dutch hospitals, the cumulative incidence of venous or arterial thromboembolism was 31%, despite all patients receiving at least prophylactic doses of anticoagulation.⁶ 81% of those

events were pulmonary embolism and none of the patients had disseminated intravascular coagulation (DIC). In contrast, 5.9% of hospitalized patients with pandemic H1N1 Influenza developed arterial or venous thromboembolism.⁷

- DIC appears to be common in fatal cases of COVID-19 and rare among those that survive, though the actual incidence is still unclear. In a retrospective study of 183 COVID-19 patients in a Wuhan hospital, 71.4% of non-survivors developed DIC during hospitalization compared to only 0.6% of survivors.¹ In another retrospective study of 225 patients in Wuhan, DIC occurred in 6.4% of non-survivors and 0% of survivors.⁸

Diagnosics & Surveillance

How is SARS-CoV-2 detected by RT-PCR (reverse transcriptase - polymerase chain reaction)?

- Shortly after sequencing of SARS-CoV-2 was completed in Wuhan, China¹ the WHO determined several core gene targets that are currently used in laboratory developed testing (LDTs): RNA-dependant RNA polymerase (RdRp), envelope (E), nucleocapsid (N), and open reading frame (ORF1) genes.²
- Detection of these genes constitutes a cycle threshold (Ct) that is used to quantitate each PCR assay. Studies from centers in Wuhan, China have reported Ct values in symptomatic patients ranging from 16-38,^{3,4} with no significant differences between symptomatic and asymptomatic patients.⁵ It is important to note that RT-PCR is a semi-quantitative test (a set Ct value determines whether a result is positive or negative), while the reported results is qualitative (positive, negative, inconclusive).
- Initially, detection of 2-3 gene targets was required to confirm positivity, but with proper validation, most countries have adopted a single target approach thus simplifying the test and reducing the required reagents.⁶ The use of sample pooling has also dramatically increased testing capacity in most centres, especially for community monitoring.⁷
- In recent months, many companies have developed platforms to automate LDTs and improve throughput. Canada has authorized 13 PCR-based detection systems to date.⁸ The Spartan Cube was most recently approved by Health Canada and it may help provide rapid diagnostics that would be particularly helpful for remote locations.⁹ Scientists at Canada's National Microbiology Laboratory are currently validating its diagnostic use.

Are any inflammatory markers indicative of prognosis in COVID-19?

- Studies have shown the CRP, ESR, and ferritin are significantly higher in severe cases of COVID-19 than moderate cases.^{1,2,5}
- Elevated IL-6 predicts clinical deterioration and correlates with the development of “cytokine storm”.^{3,4,5} This is why anti-IL-6 monoclonal antibodies are being considered in some clinical trials for treatment of COVID-19 (see [March 27, 2020 newsletter](#)).
- It is also worth noting that increased procalcitonin values have been associated with severe cases. It is not yet clear whether this is reflective of a bacterial superinfection.^{5,6}

Therapeutics

Does the BCG vaccine mitigate COVID-19?

- The Bacille Calmette-Guérin (BCG) vaccine is speculated to have protective effects against SARS-CoV-2 infection due to its non-specific immune-boosting effects, termed “trained immunity”.¹
- Recent epidemiological studies in preprint have demonstrated a possible association between neonatal BCG vaccination and lower rates of COVID-19 attributable deaths.^{2,3,4,5}
- Currently the WHO does not recommend BCG vaccination for prophylaxis against SARS-CoV-2 because these studies are limited by possible confounder bias and case ascertainment bias. Caution is important since redistribution of the BCG vaccine could be detrimental to TB endemic countries.⁶
- The WHO is planning for further recommendations based on the findings of two ongoing randomized controlled trials investigating the efficacy of prophylactic BCG administration in healthcare workers exposed to COVID-19.^{6,7,8}

What is the evidence for heparin and other anticoagulants to prevent thrombotic complications of COVID-19?

- Current Canadian guidelines recommend VTE prophylaxis in hospitalized patients with COVID-19, as per standard of care, with preference for low molecular weight heparin (LMWH). LMWH is preferred over novel oral anticoagulants (NOACs) and warfarin due to superior outcomes among critically ill patients, less drug-drug interactions, and a hypothesized anti-inflammatory effect.^{1,2}

- One group found rates of thrombotic complications in COVID-19 patients approaching 31% despite heparin prophylaxis. However, further research is needed to warrant a deviation from standard prophylaxis.³
- A retrospective review of 449 COVID-19 patients found no difference in mortality between patients taking heparin and those who did not. However, high-dose heparin was associated with mortality reduction among patients with significantly elevated D-dimer and signs of “sepsis-induced coagulopathy”. The latter includes alterations in prothrombin time, platelet count, and sequential organ failure assessment.⁴
- International guidelines suggest heparin or LMWH prophylaxis for all admitted COVID-19 patients, not just the critically ill.⁵
- No results are yet available from large RCTs that assess the efficacy of different therapeutic anticoagulation regimens in COVID-19.

Over the last few weeks, new evidence has emerged on hydroxychloroquine in the treatment of COVID-19. What do these studies show?

- A RCT involving 62 patients studied hydroxychloroquine for mild COVID-19 pneumonia and reported significant radiologic improvement, but only a small, albeit statistically significant, clinical benefit (one day reduction in duration of fever and cough).¹
- A retrospective chart review comparing outcomes of COVID-19 patients with or without hydroxychloroquine within 48 hours of hospitalization found no difference in mortality or critical illness.²
- The high-dose chloroquine arm of a clinical trial that combined chloroquine with azithromycin in hospitalized COVID-19 patients was terminated early due to increased mortality (two deaths from ventricular tachycardia) and cardiac toxicity (QTc >500 ms in 25%).³
- A case series of patients treated with hydroxychloroquine and azithromycin failed to show improved viral clearance or clinical benefit.⁴

Infection Prevention & Control

What is the efficacy of eye protection in preventing transmission of SARS-CoV-2?

- Some patients with COVID-19 have developed conjunctivitis, although their route of acquisition is unknown.¹
- The eyes can be a portal of entry for respiratory viruses. A study of intubations during the 2003 SARS outbreak found that inadequate eye protection was a

significant risk factor for healthcare worker acquired infection.² In a laboratory setting, it has been shown that eye protection can prevent transocular acquisition of aerosolized viruses.³ Outside of aerosol generating procedures, the benefit of eye protection has not been established as clearly, but it is a reasonable precaution.

- **Bottom line:** Eye protection is recommended (i.e. goggles, face shield, or mask with visor) in combination with other appropriate PPE when providing routine care to patients with COVID-19 patients and is critically important during aerosol generating procedures (see [Manitoba PPE guidelines](#)).

Does N95 fit testing matter?

- Yes! The protection provided by N95 respirators is increased when proper fit testing is instituted.¹ Studies of different N95 mask types in different populations report wide variations in the percentage of tested people with effective protection (the pass rate). Mask are certified based on their filtering, but not based on fit, and when several models are trialled the pass rate for any model is often under 50%.^{2,3} However, when workplaces choose a model based on experience in their population, the pass rates are generally very high (>85%), and only a limited number of alternative options are needed.² Thus, the likelihood of protection from using a hospital's chosen model is likely much higher than an off-the-shelf alternative.
- Unfortunately, user-seal checks have low accuracy in predicting protection.³
- A substantial benefit of mask fit testing programs is that training and practice in proper donning of N95 respirators leads to significantly more people being protected by a particular mask type.⁴ See video on donning training for [3M: 1870 mask](#), one of the N95 respirators available in Manitoba facilities.
- **Bottom line:** Shared Health recommends only using the respirator make, model, and size for which fit testing has been completed.

The following are updates on questions initially answered on [March 27, 2020](#):

Which mask/respirator is better for COVID-19 patient care?

- To date, there is no evidence to suggest that surgical masks are inferior to N95 respirators in protecting healthcare workers from infection during non-aerosolizing patient interactions.¹ This supports the current guideline that N95 respirators should be worn during aerosol-generating medical procedures and surgical masks for all other patient care.

Are there any updates on the decontamination of N95 respirators?

- This is an active area of ongoing research. One method, the Battelle Decontamination System, has been authorized in the USA as an emergency

measure to decontaminate N95 respirators via vapour phase hydrogen peroxide (VPHP).¹ The 480 minute decontamination process maintains adequate fit and filtration of the tested N95 brand for up to 20 cycles.² Research at the University of Manitoba has similarly shown that the structural and functional integrity of N95s is maintained for up to 10 cycles of decontamination with VPHP or autoclaving.³

- No effective methods of N95 decontamination that can be employed at home have been published.

Are there any updates on the efficacy of cloth masks?

- Cloth masks are now recommended in public to prevent the spread of virus from asymptomatic carriers. No clinical data is available on the effectiveness of this approach, but evidence from experimental settings suggest it may reduce viral transmission, if used together with hand hygiene and physical distancing.¹
- The filtering efficiency of cloth masks depends on fabric composition, particles to which the mask is exposed, and seal.² Washing and drying have been shown to decrease filtering efficiency³ and thus, cloth masks should be replaced after multiple uses.
- The CDC has provided [tutorials](#) on making homemade masks using cotton fabric.

Public Health Interventions

What is the evidence on how to prepare for and manage outbreaks in fly-in or remote communities?

- There are currently no specific studies focused on ways of reducing the impact of COVID-19 on remote communities. Cases of COVID-19 have been reported in First Nation communities in Ontario and British Columbia.^{1,2}
- There has been research on Influenza epidemics in remote settings and is potentially applicable to the current pandemic. Experience with H1N1 Influenza has shown that remote communities and especially Indigenous communities are very vulnerable to pandemics.³ Some of the most common barriers that promote high infection rates are overcrowded housing, insufficient human and financial resources, and inadequate community awareness.⁴
- It has been noted that general strategies used for pandemic control (social distancing, isolation of cases and their contacts, and testing)^{5,6} may be effective in remote communities, but may require modification. Close cooperation with the communities has been recommended to address their specific challenges.⁴

- As the shortage of human resources becomes more apparent with the current pandemic, more technology based measures, such as telehealth,⁷ may find their roles expanded.

What are the strategies to assist individuals living in overcrowded housing to comply with self-isolation?

- General strategies for reducing risk of secondary infection in household contacts was discussed on [April 3, 2020](#).
- Secondary transmission rates of COVID-19 among household contacts is up to 30%.¹ The R_0 (reproduction value) increases with more members and time spent in the household, which is significant in overcrowded housing.²
- Interventions to assist individuals living in overcrowded housing include:
 - (1) Evaluate the safety of current housing.³ If possible, improve housing conditions to allow for appropriate, healthy behaviors. For patients with confirmed or suspected COVID-19, this involves arranging a separate room and bathroom for their use or cohort self-isolating individuals in a shared space.⁴ Aim to maximize proper ventilation, sanitation, and physical distancing from others.
 - (2) Relocate the individual requiring self-isolation outside of the home.⁴ Mainland China and Hong Kong have created quarantine centers using vacant infrastructure (e.g. holiday villages, hotels, and gymnasiums) for individuals to self-isolate.^{5,6} Policies and conditions of centers have varied. China has related this measure to its success in controlling the outbreak, but specific data regarding its effectiveness is limited.

What strategies can be used to help prevent transmission of SARS-CoV-2 amongst people without a fixed address?

- Individuals with no fixed address (NFA) have high rates of respiratory infection.^{1,2,3} For example 3.4% of deaths of adults with NFA in New York City from 2001-2003 were caused by Influenza or pneumonia.¹ The NFA population is at risk for SARS-CoV-2 infection due to lack of access to soap and water for hand washing, overcrowding at shelters, lack of access to a telephone for telehealth appointments, and high rates of chronic disease.^{4,5}
- There are three distinct groups of people who need a place to isolate during the COVID-19 pandemic: (1) people awaiting test results or isolating after contact with a COVID-19 case, (2) people with mild cases of COVID-19 that do not require hospitalization, and (3) people >65 years old or with medical comorbidities.

- The following strategies have been suggested to help prevent the spread of SARS-CoV-2 in this vulnerable population:
 - Communication with shelters to prevent losing people to follow-up after COVID-19 testing or for contact tracing.⁶
 - Elimination of maximum stay durations at shelters to prevent guests from moving from one shelter to another and thereby decreasing the number of possible exposures.^{6,7}
 - Outreach clinics have been shown as effective ways to reach the NFA population.^{4,5}
 - Training shelter staff on how to screen for COVID-19 and providing them with testing kits.⁴ Also, provide shelters with PPE.⁶ In Toronto, a recent SARS-CoV-2 outbreak at a shelter infected 11 guests and 12 staff.⁸
- Some of the strategies currently in place in Manitoba include:
 - Shelters have been trained on how to screen for COVID-19, and the province is working on helping them access appropriate PPE.
 - In Winnipeg, a 39-unit apartment block opened to provide a place to self-isolate while waiting for test results.⁹
 - In Brandon a shelter has partnered with a motel to house and feed individuals with chronic disease and those over 65 who need to protect themselves from the virus.¹⁰

To what degree do non-pharmaceutical public health interventions affect the epidemic curve?

- In the 1918 Influenza Pandemic, lower death rate was associated with earlier closure of schools and banning of public events in the US cities.¹ The median duration of these closures were 4 weeks (range 1-10 weeks). However, it is difficult to apply the required duration of intervention for COVID-19 as its incubation period is longer than Influenza (approximately 7-14 days versus 1-5 days).
- Modeling data showed that in a society like Singapore, a combination of regulations including quarantine, school closure, and workplace distancing could reduce the number of infected patients with COVID-19 by 78.2% (assume $R_0 = 2.5$), 93.0% (assume $R_0 = 2.0$), and 99.3% (assume $R_0 = 1.5$) in 80 days.²
- A modeling study using data from Ontario (based on a $R_0 = 2.3$) found that ICU resources would be overwhelmed without either (1) substantial physical distancing (i.e.: contact reduced by 60%) or (2) a combination of moderate physical distancing (i.e.: contact reduced by 25%) with enhanced case finding.³ The model propose a dynamic scenario where public health interventions are activated when approximately 40% of ICU beds are filled with patients with COVID-19. They

suggest that using a dynamic scenario could maintain health system capacity while allowing periodic psychological and economic respite for the population.



Pediatric Corner

What is the recommendation for routine childhood vaccines during the COVID-19 pandemic?

- The Canadian Paediatric Society (CPS), CDC, and WHO all recommend the continuation of routine immunizations during the COVID-19 pandemic.^{1,2,3} Be aware of any missed vaccines that would have normally been given in school-based vaccination programs and provide catch-up as soon as possible.¹
- The CDC and WHO recognize that context is important and, in some circumstances, routine immunizations may not be possible. When only limited well-child visits are possible, the CDC recommends the prioritization of newborn care and vaccination through 24 months of age.^{2,3}
- The CPS and CDC outline ways that clinicians may prevent spread where in-person visits are unavoidable including scheduling well visits earlier in the day and sick visits later in the day, dedicating specific rooms for well visits, and limiting the number of people accompanying patients.^{1,2}
- The WHO advises increased surveillance of vaccine preventable diseases and the need to have strategies for catch-up vaccination.³ Disruption to immunization programs during a pandemic can lead to outbreaks of vaccine preventable diseases. For example, following a recent Ebola outbreak, there was a measles outbreak in a region of Guinea.^{4,5}

How can we communicate with children about the COVID-19 pandemic?

- Experts recommend that clinicians and parents begin by asking children what they understand about the COVID-19 pandemic, ensuring to correct any false information/beliefs that the child may have.^{1,2,3,4} Simple, age appropriate explanations should be provided. In particular, children need explanations regarding the rationale for changes in their routines and structures. Any questions posed by children should be answered honestly with credible information.
- Clinicians can recommend that parents: (1) teach their children when and how to wash their hands, (2) encourage them to do their part to flatten the curve, (3) limit

their children's consumption of COVID-19 related media, and (4) try to maintain a household routine while modeling healthy coping behaviours.^{1,2,3,4}

- Clinicians and parents should monitor children and teens for signs of anxiety and/or depression and seek professional assistance as needed, especially for children with pre-existing mental illness.^{1,2} Resources for children's mental health include: [AbilitiCBT for 16+ years](#) in Manitoba, and [Kids Help Phone](#).

The information presented reflects the data that is currently available to us. In the context of a pandemic where rapid dissemination of information is essential, we have included information from evolving medical literature which may be awaiting peer-review.

This report was produced by a collaboration of fellows, residents, medical students, faculty leads, and librarians from the University of Manitoba and the Medical Microbiology and Infectious Diseases community.

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